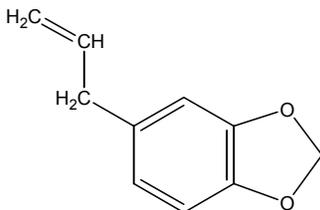


SAFROLE
CAS No. 94-59-7

First Listed in the *Second Annual Report on Carcinogens*



CARCINOGENICITY

Safrole is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC 1976). When given by gavage followed by dietary administration, safrole increased the incidences of liver cell tumors in mice of both sexes. When administered in the diet, safrole increased the incidences of liver hepatocellular carcinomas and cholangiocarcinomas in rats of both sexes, and hepatocellular carcinomas in male mice. When administered to infant mice by subcutaneous injection, safrole induced lung adenomas and adenocarcinomas in mice of both sexes and hepatomas in male mice (IARC 1976).

No adequate human studies of the relationship between exposure to safrole and human cancer have been reported (IARC 1976).

PROPERTIES

Safrole is a clear, colorless to slightly yellow liquid with an odor of sassafras. It is insoluble in water and glycerol, slightly soluble in propylene glycol, and very soluble in ethanol, ether, acetone, and chloroform. Safrole is combustible when exposed to heat or flame, and when heated to decomposition it emits acrid smoke and fumes (IARC 1976, HSDB 2001, NTP 2001).

USE

Safrole, a naturally occurring substance, has been used as a flavoring agent in drugs, beverages, and foods, and in the manufacture of heliotropin and piperonyl butoxide. Safrole has also been used in soap and perfumes. Oil of sassafras, which contains safrole, was formerly used to flavor some soft drinks, such as root beer. However, as of 1960, this use was no longer permitted in the U.S. (IARC 1976, HSDB 2001).

PRODUCTION

Safrole is produced by distillation of oils rich in safrole. Chem Sources (2001) identified seven current U.S. suppliers of safrole. U.S. production was 258,000 lb and 278,000 lb in 1969 and 1970, respectively, but was only 12,000 lb in 1977 (IARC 1976, HSDB 2001). The 1979 TSCA Inventory identified four companies producing 2.8 million lb of dihydrosafrole, three companies producing 55,000 lb of isosafrole, and four companies importing 1,000 lb (TSCA

1979). Approximately 36,000 lb of safrole were imported from Brazil in 1980 (HSDB 2001). No current import or export data were found.

EXPOSURE

Minimal exposure to safrole may occur through the use of edible spices, including nutmeg and mace, which contain low levels of naturally occurring safrole (IARC 1976, HSDB 2001). Potential occupational exposure to workers handling safrole may occur through dermal contact. Health professionals, such as pharmacists, physicians, and nurses may possibly be exposed during formulation, preparation, administration, or clean-up of drugs containing safrole or sassafras. The National Occupational Exposure Survey (1981-1983) estimated that 6,475 workers were potentially exposed to safrole in the U.S. (HSDB 2001). In 1981, OSHA estimated that 30 workers were possibly exposed to safrole. The Toxic Chemical Release Inventory listed four industrial facilities that released a total of 9,526 lb of safrole in 1999; however, 97% of the total released was from one facility (TRI99 2001).

REGULATIONS

EPA has promulgated standards for voluntary cancellation of safrole in pesticide products under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). EPA permitted one registrant to distribute and sell one safrole-containing product until 3/11/78, but after that no stocks were available for pesticide use. EPA regulates safrole under the Resource Conservation and Recovery Act (RCRA) and the Superfund Amendments and Reauthorization Act (SARA). RCRA designates safrole as a hazardous constituent of waste and it is subject to reporting rules under RCRA and SARA. A reportable quantity (RQ) of 100 lb has been established by EPA under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA).

FDA banned the use of oil of safrole and sassafras bark in food, but permits use of edible spices, such as nutmeg and mace, which contain very small quantities of naturally occurring safrole. FDA is reviewing the use of safrole in sleeping aids and sedatives.

OSHA regulates safrole under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 159.

REFERENCES

Chem Sources. Chemical Sources International, Inc. <http://www.chemsources.com>, 2001.

HSDB. Hazardous Substances Data Bank. Online database produced by the National Library of Medicine. Safrole. Profile last updated August 9, 2001. Last review date, May 16, 1996.

IARC. International Agency for Research on Cancer. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Some Naturally Occurring Substances. Vol. 10. 353 pp. Lyon, France: IARC, 1976.

NTP. National Toxicology Program. NTP Chemical Repository. Safrole. Last updated August 13, 2001. (<http://ntp-server.niehs.nih.gov> and search 94-59-7).

TRI99. Toxic Chemicals Release Inventory 1999. Data contained in the Toxic Chemical Release Inventory (TRI). Available from the U.S. Environmental Protection Agency Office of Environmental Information, <http://www.epa.gov/triexplorer/reports.htm>, 2001.

TSCA. Toxic Substances Control Act, Chemical Substance Inventory, 1979: public record.